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C. Stephens
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Patent
Attorney's Docket No. 002010-137

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	)	Box AF
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Eugene D. THORSETT, et al.	)	Group Art Unit: 1624
	)	
Application No.: 09/126,096	)	Examiner: Deepak R. RAO
	)	
Filed: July 30, 1998	)	Confirmation No.: 8518
	)	
For: COMPOUNDS WHICH INHIBIT LEUKOCYTE ADHESION MEDIATED BY VLA-4	)	

REPLY PURSUANT TO 37 C.F.R. § 1.116

Mail Stop AF
Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This Reply Pursuant to 37 C.F.R. § 1.116 is in response to the final Office Action (paper no. 29) mailed on February 4, 2003 for the above-identified patent application. This final Office Action set a three (3) month period for response and this Reply and Amendment is being filed on or before its due date of May 4, 2003 (May 4th being a Sunday, this response is due May 5th).

Withdrawal of Rejections

Applicants note that the rejections under 35 U.S.C. § 112, second paragraph, 35 U.S.C. § 102(e), and 35 U.S.C. § 102(e)/103(a) have been withdrawn.

Double Patenting Rejection

Claims 1-4, 7, 10, 12, 13 and 15-22, all of the claims remaining in this application, stand provisionally and finally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over Claims 1-35 of U.S. Patent

6,492,421 (hereinafter the '421 patent).[1] Applicants traverse this rejection for the following reasons.

Initially, for all of the reasons set forth in the Response to Office Action filed November 26, 2002, Applicants maintain that the U.S. Patent and Trademark Office has failed to meet its burden to make a *prima facie* case of obviousness.

Specifically, Applicants maintain that the Examiner has failed to provide any evidence that a person of ordinary skill in the art would be motivated to make the substitution of an α-substituted amino acid with an α,α-disubstituted amino acid. "That motivation may not be abstract, but practical, and is always related to the properties or uses one skilled in the art would expect the compound to have, if made."[2] In point of fact, the Examiner has yet to address this issue. The Examiner has merely asserted that the compounds are homolog and such an assertion is not sufficient to make a *prima facie* showing.

Secondly, the final Office Action asserts that Applicants prior reliance on *In re Coes*,[3] *In re Langer*,[4] and *In re Lalu*,[5] is misplaced. That is to say that the Office Action maintains that *In re Coes*, *In re Langer* and *In re Lalu* do not support Applicants assertion that even if the compounds of the '421 patents are deemed homologs of the claimed compounds, such homology does not create a *prima facie* case of obviousness. Applicants disagree.

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[1] Applicants submit that since the rejection is based on an issued patent, the provisional nature of this rejection should be withdrawn.

[2] In re Gyurik, 201 USPQ 552 (CCPA 1979).

[3] In re Coes, 81 USPQ 369 (CCPA 1949)

[4] In re Langer, 175 USPQ 169 (CCPA 1972)

[5] In re Lalu, 223 USPQ 1257 (CAFC 1984).

In re Coes, held that the prior art ether compound:

$$ClCH_2CH_2OCH_2CH_2OCH_2CH_2Cl$$

created an unrebutted prima facie case of obviousness against the claimed acetal compound:[6]

$$ClCH_2CH_2OCH_2OCH_2CH_2Cl$$

because the prior art was a homologue of the claimed compound differing only by a $-CH_2-$ unit (i.e., $-CH_2CH_2-$ versus $-CH_2-$) ***and*** because acetals have similar chemical properties to ethers.[7] However, nothing in Office Action establishes that α,α-disubstituted amino acids of this invention have the same chemical properties of α-substituted amino acids and Applicants submit that they do not. For example, Salgado, et al., recites that peptides containing α,α-disubstituted amino acids confer conformational rigidity and resistance to enzymatic hydrolysis as compared to peptides containing α-monosubstituted amino acids.[8] In view of these differences, the mere allegation of homology in the final Office Action should not, by itself, establish a *prima facie* case of obviousness.

As to *In re Langer,*[9] this case held that obviousness must be established against the invention "as a whole" and that rules such as homology cannot, by themselves, be used as a

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[6] In re Coes, 81 USPQ at 371, (concluding that the claimed compound was obvious and in the penultimate paragraph at page 371 concluding that the data in the application did not substantiate patentability (i.e., rebutted the *prima facie* case)).

[7] *Id.* page 371.

[8] Salgado, et al., *Enzyme-mediated Synthesis of (1S)-1-amino-2,2-dimethylcyclopropane-1-carboxylic acid,* FOURTH INTERNATIONAL ELECTRONIC CONFERENCE ON SYNTHETIC ORGANIC CHEMISTRY, September 2000 (available at http://www.unibas.ch/mdpi/ecsoc-4/a0024.htm).

[9] *Supra*, note 2.

basis to render a *prima facie* case of obviousness.[10] The assertion in the final Office Action that because this case was limited to hindered amines versus unhindered amines it was not germane to this case, is simply in error. The court in *In re Langer* held that it is important to show obviousness to the invention "as a whole" and thus viewed the Applicants invention as the use of sterically hindered amines as opposed to unhindered amines.[11] The same analysis in the present case necessitates a determination of whether that the claimed α,α-disubstituted amino acids, when viewed as a whole, are obvious over the α-substituted amino acids of the '421 patent.[12] Such has not been done.

As to *In re Lalu*, the the court held that an obviousness analysis requires an inquiry as to whether there is anything in the prior art reference which would suggest the properties of the claimed compounds.[13] Applicants submit that *In re Lalu* is germane to the facts in this application as there is nothing in the '421 patent that would suggest the properties of the α,α-disubstituted amino acids, and as such, there is no motivation to make the presently claimed compounds.

Lastly, the final Office Action recites *In re Deuel*, to support its position that the claimed compounds are *prima facie* obvious over the '421 patent.[14] Applicants maintain that such reliance is misplaced. Specifically, *In re Deuel* is directed to the question of whether cDNA molecules that encode heparin-binding growth factors are obvious over references disclosing known methods of making the molecules.[15] In deciding that case, the court recited with approval language directly from *In re Lalu* that:

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[10] *Supra,* note 2 at 171.

[11] *Supra*, note 2 at 171.

[12] This invention, as a whole, includes the α,α-disubstituted amino acids *per se*, pharmaceutical compositions comprising these compounds as well as methods of use using these compounds.

[13] *Id.* at 1260.

[14] In re Deuel, 34 USPQ.2d 1210 (CAFC 1995).

[15] *Id.* at 1214.

> The prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular modifications needed to arrive at the claimed compounds.[16]

Such a recitation is contrary to any formulaic rules and, accordingly, supports Applicants position that a mere assertion of homology is insufficient to create a *prima facie* case of obviousness absent any evidence that such homology would motivate the skilled artisan to make the necessary modifications.

In view of the above, Applicants maintain that this rejection is in error and, accordingly, withdrawal of this rejection is requested.

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[16] *Id.* at 1215.

Conclusion

In view of the above, Applicants submit that this application is now in condition for allowance. A notice to that effect is earnestly solicited. Notwithstanding the above and in order to avoid unintended abandonment of this application, a Notice of Appeal is enclosed.

In the event that a telephone conversation could expedite the prosecution of this application, the Examiner is requested to call the undersigned at (650)622-2300.

Respectfully submitted,

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Date: May 5, 2003